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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/560,727

10/10/2006

Yechiel Shai

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8544

23405

7590

09/08/2008

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EXAMINER

LUKTON, DAVID

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

09/08/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/560,727	Applicant(s) SHAI ET AL.	
	Examiner DAVID LUKTON	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) 8, 11-14 and 16-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9 and 10 is/are rejected.
- 7) ☒ Claim(s) 15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Pursuant to the response filed 5/15/08, claims 1, 18, 39, 48, 53 have been amended.

Claims 1-55 remain pending.

Claims 1-7, 9, 10, 15 are examined in this Office action. Claims 8, 11-14, 16, 17, 18-55 remain withdrawn.

Applicants' arguments filed 5/15/08 have been considered and found persuasive. The previously imposed rejections are withdrawn.



The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9 and 10 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims require that the activity (antibacterial, antifungal or anticancer) of the acylated peptide be higher than that of the deacylated peptide. And this is on top of the skilled peptide biochemist having to determine which lipopeptides will exhibit the

Art Unit: 1654

activity (antibacterial, antifungal or anticancer) in the first place. Thus, one must begin with an infinite array of lipopeptides, then determine which of them exhibit antibacterial, antifungal or anticancer activity. For each of those that exhibit the activity, one must then remove the fatty acyl group, and measure the activity (antibacterial, antifungal or anticancer) of the deacylated peptide, and then determine which of those deacylated peptides exhibit lower activity than the corresponding acylated peptide. The assertion here is that to do all of this for an infinite number of peptides would required “undue experimentation”.

Consider first Clark C. R. (*J Med Chem.* **30**(7), 1214-18, 1987) which discloses that acylation of the amino group of compound 1 eliminated anticonvulsant activity. It is true that anticonvulsant activity is not the same as antimicrobial or antitumor activity, but it does support the proposition that pharmacological activity is often eliminated when a compound is acylated. Consider also the following:

- Creemer L. C. (*J Med Chem.* **39**(25), 5021-4, 1996) discloses that acetylation of compound 7 eliminated antitumor activity.
- Uehara Y (*Journal of Antibiotics* **29**(9), 937-943, 1976) discloses that acylation of negamycin results in loss of antibacterial activity.
- Schott H (*Anti-Cancer Drug Design* **11**(6), 451-62, 1996) discloses (e.g., table V; page 459, lines 8-9) that compound 11 was inactive in an assay of anti-tumor activity. This constitutes an example of a case where conjugation of a pharmacologically active anti-tumor agent to a lipophilic group resulted in a reduction of activity.
- Trani A [*Farmaco (Societa Chimica Italiana*: 1989), **51**(7), 503-512, 1996]

Art Unit: 1654

discloses (table I, page 508) that acylation of purpuromycin causes a reduction in antimicrobial potency. Compare, for example, compound 1 with compounds 4 and 5.

- Avrahami (*Biochem* **41**, 2254-63, 2002) discloses that N-palmitoyl magainin is no more effective than magainin itself against *C. albicans* and *A. fumigatus*.

Thus, even if it were possible to determine, **absent undue experimentation**, which lipopeptides will exhibit antibacterial, antifungal or anticancer activity, one would still be left with the fact that removal of the acyl group **does not predictably result** in a reduction of activity as the claims require.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

Accordingly, "undue experimentation" would be required to practice the claimed invention.



Claim 1 is objected to on grammatical grounds. The following phrase is recited:

"...the peptide prior to conjugation being **devoid**... very weak antibacterial and antifungal activity".

Art Unit: 1654

Here, the preposition “of” should follow “devoid”, i.e.:

devoid of ... antibacterial... activity



No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

/David Lukton/

Primary Examiner, Art Unit 1654